# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/835,523 | 04/17/2001 | Yong-Qian Wu | 23754X | 5679 |

29728 7590 10/07/2004

GUILFORD PHARMACEUTICALS C/O
FOLEY & LARDNER
3000 K STREET, NW
WASHINGTON, DC 20007-5143

| EXAMINER | |
|---|---|
| KIFLE, BRUCK | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1624 | |

DATE MAILED: 10/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/835,523 | WU ET AL. | |
| | Examiner | Art Unit | |
| | Bruck Kifle, Ph.D. | 1624 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *11 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-40 and 48-51* is/are pending in the application.

4a) Of the above claim(s) *5,6,11-40 and 49-51* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,7-10 and 48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/23/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

This application has been assigned to a new Examiner. Applicant's amendments and remarks filed 8/11/04 have been received and reviewed. Claims 1-40 and 48-51 are pending in this application.

Claims 5, 6, 11-40 and 49-51 are withdrawn from consideration.

Claims 1-4, 7-10 and 48 are under consideration.

***Claim Rejections - 35 USC § 112***

Claims 1-4, 7-10 and 48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

i) It is unclear which ester or solvate is being claimed in the phrase "ester or solvate thereof."

ii) In the definition of $R_1$, the phrase "wherein said $R_1$ group is either unsubstituted or additionally substituted with $R_3$" is present. This is not consistent with the definition of $R_1$. Deletion is suggested.

iii) In the definitions of $R_2$ and $R_3$, The terms "carbocycle", "heteroaryl" and "heterocycle" are indefinite because it is not known how many atoms make up the ring and what kind of a ring is intended (monocyclic, bicyclic, spiro, fused, bridged, saturated, etc.) by carbocycle. The term "heteroaryl" is indefinite because it is not known how many atoms are present, how many and what kind of heteroatoms are involved, what size ring is intended and how many rings are present. The term "heterocyclic" is indefinite because it is not known how many atoms make up the ring, which atoms are present and what kind of a ring (monocyclic, bicyclic, spiro, fused, bridged, saturated, etc.) is intended.

iv) The groups "thiocarbonyl" and "carbonyl" are open ended because they have an open valency.

v) It is unclear what is accomplished by claim 7. Who is in need of "affecting a neuronal activity" and who is not?

Claims 1-4, 7-10 and 48 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a pharmaceutical salt, does not reasonably provide enablement for solvates of the compound of formula I. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. Applicants have not shown how one skilled in the art can arrive at a given solvate. None of the compounds made are crystallized out as solvates. Arriving at a given solvate is not routine experimentation because it is unpredictable. One cannot make any solvate a given compound.

Claims 7-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for "affecting a neuronal activity", "preventing neurodegeneration", "treatment of a neurological disorder" and treating or preventing Alzheimer's disease, Huntington's disease or ALS.

In evaluating the enablement question, several factors are to be considered. Note In re Wands, 8 USPQ2d 1400 and Ex parte Forman, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art,

4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

1) The nature of the invention: The method of use claims are drawn in part to prevention and treatment of any and all neurodegenerative conditions, affecting any and all neuronal activity, etc.

2) The state of the prior art: There are no known compounds of similar structure which have been demonstrated to prevent or treat neurodegeneration generally. There are no known compounds which affect a neuronal activity generally.

Claim 7 is drawn to affecting a neuronal activity. This claim would read on affecting a neuronal activity in mammals with below normal, normal or above normal neuronal activity. Affecting a neuronal activity in asymptomatic mammals with normal, below normal or above normal neuronal activity. The specification fails to teach any benefit to be gained from such actions. Is extensive experimentation required on the part of a potential infringer to determine if his use of Applicants' compounds falls within the limitations of applicants' claim? *In re Kirk and Petrow*, 153 USPQ 48 (CCPA 1967). As the Supreme Court said in *Brenner v. Manson*, 148 USPQ at 696: "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." As U.S. Court of Customs and Patent Appeals stated *In re Diedrich* 138 USPQ at 130, quoting with approval from the decision of the board: "We do not believe that it was the intention of the statutes to require the Patent Office, the courts, or the public to play the sort of guessing game that might be involved if an applicant could satisfy the requirements of the statutes by indicating the usefulness of a claimed compound in terms of possible use so general as to be meaningless and then, after his research or that of his

competitors has definitely ascertained an actual use for the compound, adducing evidence intended to show that a particular specific use would have been obvious to men skilled in the particular art to which this use relates."

It has been recited in claims 8-10, a method of treating or preventing neurodegenerative disorders. There is no such an agent, which can treat, much less prevent, neurodegenerative disorders generally. That is because neurodegenerative disorders are extremely varied in origin and nature of effect. The origin and the nature of many neurodegenerative disorders such as Huntington's disease, Pick's disease, Frontotemporal dementia, Cerebro-Oculo-Facio-Skeletal (COFS) syndrome (cranofacial and skeletal abnormalities), Motor neuron disease (muscle weakness), Corticobasal ganglionic degeneration, Creutzfeldt-Jacob disease (fatal disease), Dementia with Lewy bodies, and Progressive supranuclear palsy Dementia are different one from the other. Many neurodegenerative disorders are untreatable to this day.

The symptoms and nature of these diseases are also different one from the other. It can be shown that many of these neurodegenerative disorders have different origin and nature of effect. Some neurodegenerative disorders are hereditary (Charcot-Marie-Tooth disease). Many neurodegenerative disorders vary in how they affect the body and its functions. Diseases such as Cerebral palsy, and Parkinson's disease affect the movement of the patient. Diseases such as Alzheimer's disease affect the memory of the patient.

3) The predictability or lack thereof in the art: It is presumed in the prevention of the diseases and/or disorders claimed herein there is a way of identifying those people who may develop any kind of the disorders recited. There is no evidence of record which would enable the skilled artisan in the identification of the people who have the potential of becoming afflicted with the

disorders claimed herein. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

Also, see In re Surrey 151 USPQ 724, regarding sufficiency of a disclosure for a Markush group, and MPEP 2164.03 for enablement requirements in cases directed to structure-sensitive arts such as the instant pharmaceutical arts.

4) The amount of direction or guidance present and 5) the presence or absence of working examples: There are no doses present to direct one to protect a potential host from the disorders cited. There are no doses present for treatment of the disorders recited and there is no data present for the prophylaxis of these disorders.

6) The breadth of the claims: The claims are drawn to disorders that are not related and whose prevention is unknown.

7) The quantity of experimentation need would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan for the many reasons stated above.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims.

***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed.

Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-4, 7-10 and 48 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 6,417,189. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are fully embraced by the patented claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruck Kifle, Ph.D. whose telephone number is 571-272-0668. The examiner can normally be reached on 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund J. Shah can be reached on 571-272-0674. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

Bruck Kifle, Ph.D.
Primary Examiner
Art Unit 1624

BK
October 1, 2004